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TREATMENT OF TUBERCULOSIS

LETTER FROM THE SECRETARY OF THE TREASURY

TRANSMITTING

IN RESPONSE TO A SENATE RESOLUTION OF MAY 26, 1913, A REPORT BY THE UNITED STATES PUBLIC HEALTH SERVICE OF ITS INVESTIGATION OF THE METHODS AND PRACTICES EMPLOYED BY DOCTORS KARL AND SYLVIO VON RUCK IN TREATING TUBERCULOSIS AND RENDERING PERSONS IMMUNE FROM TUBERCULOSIS

DECEMBER 10, 1914.—Referred to the Committee on Public Health and National Quarantine

WASHINGTON
GOVERNMENT PRINTING OFFICE
1914

SUBMITTED BY MR. RANSDELL.

In the Senate of the United States,
December 14, 1914.

Ordered, That the letter of the Secretary of the Treasury transmitting, in response to a Senate resolution of May 26, 1913, a report by the United States Public Health Service relative to the methods and practice employed by Drs. Karl and Sylvio von Ruck in treating tuberculosis and rendering persons immune from tuberculosis be printed as a document.

Attest:

James M. Baker, *Secretary.*

LETTERS OF TRANSMITTAL.

TREASURY DEPARTMENT,
OFFICE OF THE SECRETARY,
Washington, December 9, 1914.

The PRESIDENT OF THE SENATE.

SIR: I have the honor to transmit herewith a report by the United States Public Health Service, submitted in accordance with Senate resolution 89, of May 26, 1913, providing for an investigation of the methods and practices employed by Drs. Karl and Silvio von Ruck in treating tuberculosis and rendering persons immune from tuberculosis.

Respectfully,

W. G. MCADOO, *Secretary.*

TREASURY DEPARTMENT,
OFFICE OF THE SURGEON GENERAL,
BUREAU OF THE PUBLIC HEALTH SERVICE,
Washington, November 30, 1914.

The honorable the SECRETARY OF THE TREASURY.

SIR: I have the honor to submit herewith a report of the investigation of the methods and practices employed by Drs. Karl and Silvio von Ruck in treating tuberculosis and in rendering persons immune from tuberculosis. This investigation was undertaken in accordance with the provisions of Senate resolution 89, of May 26, 1913, which reads as follows:

> *Resolved*, That the Secretary of the Treasury be, and he is hereby, requested to institute, through the Bureau of Public Health, an investigation of the practices and methods employed by Drs. Karl and Silvia von Ruck, of Asheville, N. C., in treating tuberculosis and in rendering persons immune from tuberculosis, and to report to the Senate, as soon as practicable, whether the vaccine used by the said Drs. von Ruck in attempting to render persons in health immune to tuberculosis is successful in immunizing those thus vaccinated.

The duty of conducting this investigation was imposed upon Surg. A. M. Stimson, who on July 29, 1913, was directed to proceed to Asheville, N. C., for that purpose. The selection of this officer was made because of his special technical fitness and long experience in the Hygienic Laboratory. The investigation was continued from August 6, 1913, to October 23, 1914, either at Asheville, N. C., or Washington, D. C.

On account of the significance of the claims to be investigated and the intent of the Senate to secure an authoritative expression of opinion in relation thereto, the director of the Hygienic Laboratory was associated with the work in an advisory capacity. The advisory board of the Hygienic Laboratory, whose membership includes eminent scientists connected with leading scientific institutions of the

country, was also consulted in respect to the methods of conducting the investigation, and its advice followed.

It was recognized and so stated in a letter of May 28, 1913, to the department that the investigation in respect to conferring immunity would have to be confined largely to the lower animals, and this view was concurred in by the advisory board of the Hygienic Laboratory. From correspondence and verbal statements made by Dr. Karl von Ruck, it was the understanding that the investigations desired by him could be easily carried out and that the essential object was to confirm or disprove by animal experimentation the reliability and success of his methods and practices in the production of immunity.

After beginning the studies, certain facts were elicited by Surg. Stimson which caused the methods of conduct of the investigation to become a subject of disagreement, the essential point being the right of the Government's representative to conduct an independent and uncontrolled investigation, which was objected to by Dr. von Ruck. In consequence of the Government's right in this respect being disputed, and the facilities of Dr. von Ruck's laboratory for independent research withdrawn, the work was transferred to Washington and continued in the Hygienic Laboratory. In the meantime numerous conferences and much correspondence have been had regarding the matter, and actual experimentation has been carried on for a sufficient length of time to permit the making of this report.

The investigation was undertaken and carried on with the hope that an improved agent for the prevention and cure of tuberculosis had been evolved. As the work progressed, however, it became evident that the specific claims made for the agent could not be substantiated. This opinion is based on scientific data set forth in the accompanying report.

Respectfully,

RUPERT BLUE,
Surgeon General.

REPORT ON THE INVESTIGATIONS OF THE METHODS AND PRACTICES EMPLOYED BY DRS. KARL AND SILVIO VON RUCK IN TREATING TUBERCULOSIS AND IN RENDERING PERSONS IMMUNE FROM TUBERCULOSIS.

By Surg. A. M. Stimson,
United States Public Health Service, Washington.

This report consists of an account of an investigation made by direction of the Surgeon General of the United States Public Health Service in accordance with the provisions of Senate resolution 89 of May 26, 1913.

For the sake of convenience this report is divided into two parts. In the first part the attempt is made to describe the investigation and its results in language as free as the nature of the subject will permit from intricate technical considerations which would tend to obscure the main facts from the nontechnical reader. In the second part, essentially an appendix, are contained the details of experiments, technical discussions, and quotations from the literature and correspondence, which form the basis of the first part.

Part I.

The Senate resolution literally interpreted imposes a task which under practical conditions amounts to an impossibility. It is evident that there is no absolute way in which to determine whether a person has been successfully immunized or not, except to subject the person to tuberculous infection and observe whether or not he becomes tuberculous. This experiment would have to be carried out on a large number of persons with a suitable number of untreated persons similarly inoculated, as controls, in order to make it conclusive. Such an experiment is obviously impossible.

The plan at once suggests itself of having the immunizing treatment applied to a series of persons, preferably children, and of observing these persons, together with a corresponding number of untreated persons, for a sufficient period of time to determine the relative prevalence of tuberculosis of natural origin in the two groups. In order to make such a test convincing it would be necessary to observe a large number of persons under identical conditions as regards opportunity for infection and the presence of factors which might influence resistance to infection, and this observation would have to be continued over a period of several years. These conditions are so exacting as to be impracticable, at least under the circumstances under which the present investigation has been made.

The infant science of serology has made such advances in recent years that the intelligent layman seems to be under the impression that almost any information regarding a person's physical condition can be elicited by "testing the blood." This confidence, as every serologist knows, is justified in only a few isolated instances.

As applied to tuberculosis, serology is only just beginning to show signs of emerging from a state of chaos. Standard procedures have not been generally adopted, and only partial answers can yet be given to the question as to what the relation of the reactions obtained to the condition of the patient actually is. However, certain observers have attempted to keep a check on their methods of treatment by means of serum reactions, believing that in this way their therapeutic endeavors could be more accurately carried out than by observing the physical signs of disease and noting the subjective symptoms. Among these observers are the Drs. Karl and Silvio von Ruck.

In so far as the methods of treatment of the Drs. von Ruck differ from the ordinary methods of treating tuberculosis, they consist of procedures controlled by and based upon a system of serum tests elaborated by them. They have stated also that the principles underlying their methods are readily demonstrable by experimental investigations on the lower animals. The fact that the methods peculiar to the Drs. von Ruck have been placed by them on an experimental basis affords an opportunity for investigation along laboratory lines, which has the advantages of accuracy and quickness over the purely clinical investigation. This method, however, has the drawback that it does not directly answer the question of whether a given treatment can cure or prevent tuberculosis in human beings or not.

Nevertheless, it must be recognized that if, in such an investigation, those claims, made by the originator of a method of treatment which are susceptible of laboratory demonstration, be confirmed, a degree of corroboration of his claims in general is to be inferred. On the contrary, if these claims be not confirmed, the inference is that the method in general is at fault, especially when, as in the present instance, the whole structure of the method rests upon laboratory methods as its foundation.

Inasmuch as the Senate resolution requests "an investigation of the practices and methods employed by Drs. Karl and Silvio von Ruck, of Asheville, N. C., in treating tuberculosis and in rendering persons immune from tuberculosis," I must advert briefly to those methods and practices employed by the Drs. von Ruck, which are not peculiar to them but are also recognized and used by phthisiologists generally.

The Winyah Sanatorium, at Asheville, of which the Drs. von Ruck are both proprietors and medical directors, consists of spacious and well-appointed buildings for the accommodation of patients, pleasantly and favorably located on the edge of this town, the climate of which, deservedly or not, enjoys the reputation of being advantageous for tuberculous cases. At the time of my stay in Asheville a large number of patients were being lodged in tents of a modern type erected on the grounds of the sanatorium pending the completion of additions to the main building. The food supplied appeared to be superior to that usually furnished in the better class of boarding

houses where tuberculous patients are received, both in quality and method of preparation. The two generally recognized important elements of air and food appeared to be adequately supplied at Winyah.

The medical force was probably inadequate in numbers, the ratio of patients to physicians being so great as to preclude more than the briefest individual attention. The institution was well equipped with modern therapeutic apparatus, including that for producing artificial compression of the lung. The Drs. von Ruck are intelligent men, who unquestionably have had the experience necessary for acquiring a profound knowledge of tuberculosis from a clinical standpoint.

Entirely aside from the question of the special methods of treatment employed there, the Winyah Sanatorium appears to be a well-managed institution, with the possible exception of inadequate medical force. However, it is to be inferred that the resolution does not refer especially to the general methods used by the Drs. von Ruck, but is concerned principally with the special methods which they employ, since it refers specifically to the "vaccine."

The specific methods employed by the Drs. von Ruck consist of the injection subcutaneously of one or both of two substances prepared by them from the tubercle bacillus. One of these, the watery extract, has been used for a much longer time than the other, which is designated the vaccine. The latter is considered by its originators to act in a similar manner to the former, but to constitute an important improvement in that its action is said to be more powerful and its composition more perfect. These preparations are for sale and are advertised to physicians in descriptive pamphlets with price lists. The methods of preparation and use of these products, and descriptions of the results which the authors have achieved in treating and preventing tuberculosis in man and animals, are set forth in various published articles, some of them in medical journals here and abroad and some in privately printed articles and in advertising material. These results are summarized in a letter from Dr. Karl von Ruck to the director of the Hygienic Laboratory of the Public Health Service, dated February 28, 1913, as follows:

1. That guinea pigs, rabbits, and calves can be immunized, that their blood sera destroy virulence of tubercle bacilli in vitro, and that the bacilli under the action of such sera undergo morphological changes in the test tube showing their disintegration. That such animals resist virulent infection.

2. That children and adults, after a single dose, respond with an ample degree of immunity which may be shown by biological tests for the several specific antibodies, including amboceptors and opsonins.

That their sera acquire bacteriolytic and germicidal power demonstrable in vitro, and by animal experiment, the animals resisting inoculation with the contents of test tubes in which 1/200—1/100 mgr. of virulent tubercle bacilli have been exposed to the action of such sera.

3. That tuberculous children and adults, in the truly early stage of tuberculosis and reacting to a tuberculin test, recover their general health; that physical signs become retrogressive, or disappear; that symptoms disappear, and that they no longer react to tuberculin without any further treatment after administering a single dose, and that their sera retain the bacteriolytic and germicidal power, this being demonstrable now in every case up to 20 months from the time of administering a dose.

It was to the investigation of the basis of these claims that the present inquiry was addressed.

The first two months of the investigation were spent by me at Asheville, where I was in daily attendance at the Winyah Sanato-

rium. This time I devoted almost entirely to observing the laboratory methods there employed and in conducting independent observations and experiments which were designed to act as controls on the work observed. These observations and experiments showed the methods employed by Dr. Karl von Ruck in the laboratory to be faulty and unreliable and the results of the experiments as placed on the record books misrepresented. I therefore insisted on conducting the investigation independently in accordance with the original plan.

In consequence, Dr. von Ruck summarily interrupted the investigation in Asheville by requesting me to discontinue independent investigations at his laboratory. On official instructions, the animals under my experimentation were therefore shipped to the Hygienic Laboratory, and the subsequent investigations have been carried out there. They have confirmed those made at Asheville as regards the unreliability of Dr. von Ruck's laboratory methods, and, in addition, have shown that the serum of persons supposed to have been immunized does not, as claimed, destroy the virulence of tubercle bacilli, and that it is not possible to immunize guinea pigs with the von Ruck vaccine in the manner and in the length of time claimed by the originator. The details of these investigations and their results are contained in part 2 of this report.

Inasmuch as it is the position of the department to interpret the Senate resolution as referring to what had already been accomplished by the Drs. von Ruck and not what might at some future time be accomplished, the conclusions here submitted are based upon observations made between the dates of August 6, 1913, and October 23, 1914, the period occupied by the investigation.

Part II.

The serum tests in general.—The system of specific therapeutics evolved by the Drs. von Ruck in the treatment and prevention of tuberculosis is based upon certain serological tests, elaborated but not originated by them. These are the familiar reactions of complement fixation, bacteriolysis, agglutination, precipitins, and opsonins, applied by technical procedures of their own devising. The Drs. von Ruck describe their vaccine as composed of certain fractions of the tubercle bacillus, derived by physical and chemical means, selected and brought together in accordance with the results of animal experiments. The individual fractions were injected, they say, into groups of animals separately and in various combinations, and the various serum reactions above enumerated were observed. The vaccine is supposed to represent the most effectual combination of the fractions most potent in producing the reactions which are regarded as indicative of immunity. Its constituents are adjusted with nicety and expressible in a formula. Thus, the formula for a specimen of vaccine handed me for the immunization of animals was given as—

Protein No. 1.....	0.25 mg.	Per cc. of vaccine.
Protein No. 2.....	2.75 mg.	
Protein No. 3.....	1.00 mg.	
Protein No. 4.....	6.00 mg.	
Neutral fats [1].....	0.005 mg.	
Fatty acids [1].....	0.005 mg.	

[1] The fat content of this particular specimen was said to be somewhat uncertain.

It is evident, therefore, that serum tests are the basis of the composition of the vaccine, as the latter is of the von Ruck methods for the treatment and prevention of tuberculosis. Certain observations apply to the serum tests in general as regards their significance of immunity and as to the methods of carrying out. These reactions as applied to tuberculosis have at present no settled significance which is generally accepted by students of immunity. Individual workers with particular tests have in some instances drawn conclusions as to the significance of a given test as bearing upon the condition of the patient from whom the serum was derived, his susceptibility or immunity, or the fact of his infection with tuberculosis.

These conclusions have not as yet been corroborated and accepted so that the tests applied to tuberculosis occupy anything like the position, for example, of the Wassermann reaction of syphilis. To elaborate these tests into a system of therapeutic procedure and control requires, in the light of our present meager knowledge, no little assurance.

The technic of making these tests as observed by me at Asheville was not such as to inspire confidence in the results. Only small specimens of blood were available, since Dr. von Ruck would not allow blood to be drawn from a vein, as is now the general practice, but insisted in having the specimens obtained by stabbing the finger end with a lancet and collecting the drops as they were squeezed out in a small test tube. In this way only one, or two at most, cubic centimeters were commonly secured, the serum from which, usually highly contaminated with bacteria, must suffice for all the tests to be made; complement fixation, lysin, agglutinin, precipitin, and at times opsonin. Blood was obtained from guinea pigs by laboriously milking the incised ear, was scanty in quantity, and always grossly contaminated.

The matters of cleaning and sterilizing glassware were inadequately attended to on my arrival, but improved somewhat when I insisted that what I used should be clean.

The laboratory arrangements were most inconvenient. For example, the diener service, being practically negligible, it was necessary for the laboratory workers to engage in a sheep hunt in a large field, run down their animal, and throw and hold him in order to obtain blood corpuscles for the fixation tests.

The bulk of the work demanded by Dr. von Ruck of his assistants was very large, and the assistants were obliged to work long hours daily to keep up with it. None of these men could be called a competent serologist in the sense of being a student of the subjects with which he was working, competent to form his own judgment of the propriety of the technic he was employing. These men performed the mechanical portions of the work assigned them, each according to his individual understanding or recollection of what the standard technic (if there ever had been such) of the laboratory consisted of. It was early discovered that this technic varied materially with the individual worker, as regards some of the tests; and indeed it was most difficult to obtain an authoritative statement as to what technic Dr. von Ruck desired to have followed. Only by repeated questioning of Dr. Karl von Ruck personally and the ignoring of irrelevant and evasive answers was it possible to obtain from him a description of the technic which he desired to have used in the "lytic" experiments.

The serum and reagents were handled and measured by means of nongraduated capillary pipettes provided with rubber bulbs, and it was assumed that these pipettes delivered 20 drops to the cubic centimeter. However, I observed that the pipettes were not always calibrated and that in any event the viscosity of the reagents varied so greatly that no accurate measurements were possible. In some of the tests this was relatively immaterial, but in the fixation tests which have a rigid quantitative basis it was a certain source of inaccuracy.

Owing to the miniature scale of the individual tests necessitated by the small amount of serum available, considerable error could arise from the adherence of droplets of the serum or reagents to the side of the small tubes which could not be dislodged by the small total bulk of fluid used. The water bath was not used for incubating purposes in the main tests, the small apparatus being large enough only for some of the preliminary determinations; instead, a hot air incubator was employed.

The general impression made by the tests was that of slovenly technic, and the impression did not improve on closer inspection.

One of the tenets of the von Ruck system is that the reactions noted after the administration of the vaccine vary greatly from day to day, even to the extent of being present on one day, absent on several successive days, and then suddenly present in full strength again on the following day. Although the phenomenon of daily variations in the strength of such reactions is not unknown in serology, still the extreme fluctuations claimed by Dr. von Ruck are unusual; and especially when they are said to occur in persons who have received their treatment a long time previously does the evidence on which such assumptions are based become worthy of investigation.

An examination of the records at the laboratory revealed the fact that on a given day nearly all of the results would be positive, while on another day a majority would be negative, although on both days a heterogeneous collection of specimens from persons and animals would have been examined.

This fact indicates to my mind that some difference in the technic was responsible for the apparent fluctuations. I contended, in other words, that there was no apparent reason to expect that out of an assortment of sera from persons and animals in various stages of treatment a preponderance would be positive on a given day, negative for several successive days, and then positive again on the following day while there were excellent reasons for expecting that variations of technic would give the appearance of just such fluctuations.

I do not mean by this to deny that some fluctuation in the antibody content may occur. I believe that it does occur, but I consider the evidence of the von Ruck record books incompetent to indicate the frequency, direction, and intensity of the fluctuations. This, in fact, is my attitude toward the entire evidence of the von Ruck laboratory methods, that they are incompetent to indicate the frequency, direction, and intensity of reactions which may reasonably be expected to occur. Under these conditions, the chances against such a product as the vaccine representing an ideal combination would approach infinity, since the composition of the vaccine is dependent upon the accuracy of these very factors.

I believe that any student of immunity, as familiar as is Dr. von Ruck with the literature of his subject, could evolve a vaccine theoretically as good as his own without resorting personally to experimental work.

The reaction of complement fixation.—This reaction assumes the chief rôle in the support of the von Ruck system of prophylaxis and therapeutics. Although its importance is rivaled by the phenomenon of "lysis" in his publications, this latter is deposed somewhat by statements made to me by Dr. Karl von Ruck verbally. According to the claims complement fixation was employed in determining the composition of the vaccine, and also in estimating the progress of patients under treatment, and to ascertain when experimental animals had reached a degree of immunity justifying inoculation tests with virulent tubercle bacilli.

The test as employed at the von Ruck laboratory was poor in theory and rendered worse, if possible, by poor technic in practice. In the first place, it is a *one-unit* system. The minimum amount of complement and hemolytic ambocepter is determined by preliminary titration, and the units so obtained are employed in the main test without multiplication. The hemolytic system was unsatisfactory, consisting of calf cells, sheep ambocepter, and rabbit complement. The ambocepter titer was low, necessitating large amounts of serum being used in the test, more in some instances than there was of the serum to be tested. Rabbit complement is notoriously unreliable, and was apparently responsible for some astonishingly discordant results.

During the period where, following my disapproval of the technic, a great variety of procedures was tried out under Dr. von Ruck's direction, the hemolytic system was the subject of much perturbation, and what combination was finally decided upon I can not state; but, judging from Dr. von Ruck's recent correspondence, it also has proved unsatisfactory.

The antigens employed were of Dr. von Ruck's own devising, although similar antigens have been used by other observers. Those commonly employed were designated the T. B. antigen (TB), neutral fats (NF), fatty acids (FA), and protein No. 2 (P2). Others were said to be employed at times. Some of these antigens were standardizable with great difficulty, if indeed at all with accuracy, and of themselves caused a disconcerting discoloration of the blood-containing fluid.

In view of the facts that but one unit (roughly determined) of complement was present in the test, that the antigens were of themselves anticomplementary and their standardization difficult, that a large amount of rabbit serum was present, and that the serum to be tested was usually highly contaminated with bacteria, it is not surprising that, in the *absence of or ignoring controls*, "positive" reactions could be obtained in almost any serum in which such a result was desired. When, however, it happened that the estimation of the complement unit had been generous, that of the antigen unit rigorous, when the ambocepter unit was small and the serum relatively fresh and uncontaminated, it is evident that larger amounts of the serums to be tested would be necessary to cause binding, and on a day when such conditions prevailed the percentage of positives would be small.

Why, with all his reading, Dr. Karl von Ruck had settled upon a method so fraught with sources of error, when methods much more satisfactory were already in general use, is a question difficult to answer.

Supposing that Dr. von Ruck's technic for the complement fixation test had been free from criticism, the question of the significance of his results would still remain for discussion. He apparently places great reliance on the presence of antibodies demonstrated in this manner as an index of the immunity of the person or animal furnishing the serum. The conception formed from the now rather extensive literature on complement fixation in tuberculosis and from my own studies is hardly in support of this view.

It is a fact that the majority of persons suffering from active tuberculosis have antibodies in their serum which can be shown by complement fixation tests; and further, there is evidence that as such persons improve, as the disease becomes "arrested" or "cured," these antibodies become less strong or disappear entirely.

That antibodies can be formed as the result of the injection of almost any foreign proteid is well recognized, and it would be surprising if some such action did not follow the introduction of the von Ruck vaccine. But that such antibody formation would indicate the establishment of immunity is, I believe, an assumption entirely unjustified. As in syphilis, so in tuberculosis, a positive complement fixation test usually indicates continued active disease, while persistent negative reactions indicate its absence, so far as our present knowledge will permit us to assume. The exceptions to this statement apply to the very beginning and the final stages of the disease in question.

These speculations, however, are hardly called for, since it has not been reliably shown that such antibodies are formed as the result of the von Ruck injections.

Complement fixation tests performed by the service representatives in connection with the investigation:

Dr. von Ruck repeatedly insisted that any investigator who attempted to control his methods should follow his technic, and this is my explanation of the technic used in some of the following tests. When I became convinced of the inutility of this technic I made parallel tests in some cases with a technic which I regarded as more reliable.

August 21, 1913, tests of sera of seven calves which had received a course of treatment with the vaccine.

Amboceptor determination:

Complement.	Amboceptor.	Cells.	Hemolysis ½ hr.
0.1 cc.	1/5 gtt.	1 cc.	+
0.1 cc.	1/7 gtt.	1 cc.	+=unit.
0.1 cc.	1/10 gtt.	1 cc.	±
0.1 cc.	1/20 gtt.	1 cc.	±

Complement determination:

Complement.	Amboceptor.	Cells.	Hemolysis ½ hr.
2 gtt.	1 unit.	1 cc.	+
1 gtt.	1 unit.	1 cc.	+=unit.
½ gtt.	1 unit.	1 cc.	±

Antigen units determined as follows by Dr. von Ruck's assistant: TR = 1 gtt., NF = 1 gtt., FA = 2 gtt., P2 = 2 gtt.

Serum ¼ gtt.	Main test (results in + mean hemolysis, i. e., no fixation).					
	TB.	NF.	FA.	P2.	No antigen.	
Calf 1	−	±	−	−	±	1 unit of complement to all tubes. 1 hour incubation. 1 c. c. cells added and 1 unit amboceptor. Reading after 2 hours.
Calf 2	−	+	−	−	+	
Calf 3	−	+	−	−	+	
Calf 4	+	+	−	−	+	
Calf 5	−	+	−	−	+	
Calf 6	−	+	−	−	+	
Calf 7	±	+	±	−	+	
Calf X, untreated	−	+	−	−	+	
No serum	+	+	+	±	+	

The results show that although neither the serum alone (except No. 1) nor the antigen alone (except P2) gave evidence of anticomplementary action, yet in combination they caused a restraint of hemolysis, which, however, was as marked in the case of the untreated calf as in those which had been treated. One is left to decide whether the serum of all the calves, including the untreated one, fixed complement, or whether there was something wrong with the test. Since the untreated calf gave equal apparent fixation with the rest of them, the latter appears to be the real explanation. Again, the serum of the treated calves all reacted essentially alike, although the animals had received different courses of treatment.

The von Ruck records credited all the animals with more or less antibodies, but in their series no untreated animal had been examined, this being a control which I insisted on making for my own information. How important it proved to be is apparent.

The conclusions from this test were that the finding of complement binding antibodies by Dr. von Ruck's assistants had not been confirmed, inasmuch as the controls had shown that the checking of hemolysis was due to a summation of the anticomplementary action of the serum and of the antigens and not to a true fixation This result was rendered readily possible by the fact that but one unit of complement was present in the tubes.

August 25, 1913.—Tests of sera of four children who had been given "immunizing" vaccine treatment at the Thomasville Orphanage about a year previously. A control serum from a healthy untreated person was run with these as well as salt solution controls. In this series the experiment was made of running a parallel test with two units of complement and amboceptor, in addition to the one unit system of Dr. von Ruck. The sera when presented for examination were several days old. Some degree of fixation was found by Dr. von Ruck's force in all these sera, but they did not employ the controls mentioned. My results showed apparent fixation of all the sera, including the normal control, when the one-unit system was used; but the antigens and the sera separately were shown to be anticomplementary. However, when the two-unit series was examined, a consideration of the controls did not justify the assumption of specific fixation, and it was concluded that my tests did not confirm the

finding of complement binding antibodies in the serum of these children.

September 20, 1913.—The serum of four children who had as yet not been treated was examined. The results showed no fixation which was in accord with the findings of Dr. von Ruck's assistants.

September 29, 1913.—A test was made on the sera of eight children who had as yet received no treatment. It was intended to repeat the examinations at times after the children had received immunizing doses of the vaccine, but owing to the discontinuance of the work of the service representatives at Asheville this plan was not carried out. The tests resulted negatively. At the same time the serum of a person who had received about 20 injections of the von Ruck watery extract, ending the previous March, was examined. The result was the same as in the case of the untreated children.

October 3, 1913.—A test was projected on the sera of 14 "immunized" and two untreated persons, the former having been brought to the laboratory by Dr. von Ruck's directions for the purpose. In accordance with Dr. von Ruck's desire that his methods be employed, the one-unit system was employed. The test was a long one, lasting far into the evening on account of the old difficulty of stardardizing antigens by Dr. von Ruck's methods; and when the final test was made it was found that no hemolysis had occurred, even in such controls as should have shown it, this being due to the deterioration of the complement. Thus, the effort and valuable material were lost and the test proved nothing. With the two-unit system in common use this could hardly have occurred. Owing to the scanty amount of serum available no repetition of the test could be made.

May 16, 1914.—Twenty-four sera, received from Dr. von Ruck in a Frigo apparatus and kept at a temperature of about 5° C. until the moment of examination, were subjected to complement fixation tests. This shipment was accompanied by a statement of the technic at that time in use at the von Ruck laboratory and of his results in examining the sera (which in his tests had all shown complement fixation), and by all reagents for the test with the exception of calf cells and complement. The instructions were carried out to the letter. No fixation was shown in any case.

In order to determine whether, by a more suitable technic, antibodies could be demonstrated, such specimens as there remained a sufficient amount of were tested by the technic in use at the Hygienic Laboratory, which had proved its value by demonstrating antibodies in a large percentage of tuberculous persons. By this method no fixation was shown with the von Ruck antigens, but with Calmette's peptone extract antigen, complement fixation was shown in one case (No. 52) and partial fixation in three cases (Nos. 6, 43, and 44) of the eight sera so examined. The comparison of these results with the statement of the condition of the patients made by Dr. von Ruck is perhaps sufficiently interesting to merit tabulation.

Serum No.	Fixation Calmette's antigen, Hygienic Laboratory.	Dr. von Ruck's record of the patient's condition.
6	Partial	Oct. 4, 1911.—Slight physical signs right side, subclavicular. No sputum. Apr. 5, 1912.—Lungs clear. (No recent examination recorded.)
30	None	Suspect. Some flattening. Lung examination negative.
41	do	Normal.
43	Partial	Aug. 16, 1913.—Advanced phthisis. Destructive lesions both upper lobes. Pleurisy left base. Tubercle bacilli present in sputum. May 16, 1914.—Both cavities dry; only healed lesions; to be discharged as apparently recovered.
44	do	Apr. 7, 1914.—Both upper lobes. Right side râles in apex. Many tubercle bacilli in sputum. May 6, 1914.—Moderate improvement in physical signs.
50	None	Feb. 28, 1914.—Infiltration both upper lobes. Small cavity right apex. No tubercle bacilli found. Apr. 30, 1914.—Soft-blowing expiration in right apex, near sterno-clavicular junction. Lungs otherwise clear.
52	Complete	Nov. 7, 1913.—Both upper lobes. Beginning destructive process left apex. Cavity with râles right upper. Tubercle bacilli in sputum. Apr. 17, 1914.—Greatly improved. Cavity right side almost healed. Left apex signs diminished.

It will be noticed that in three of the four cases which gave partial or complete fixation with Calmette's antigen, tubercle bacilli had been demonstrated in the sputum, while signs of more or less advanced tuberculosis were found in the lungs. In the fourth case no physical examination had been recorded for two years. In the three cases giving a negative reaction, on the other hand, tubercle bacilli had never been found. Two had no physical signs of tuberculosis, and the third presented signs which must be regarded as dubious, in the absence of tubercle bacilli, the diagnosis of cavity at the sterno-clavicular junction being frequently erroneous.

It seems evident, then, that the test was working properly, the results being consistent with those of contemporary observers; and yet when the von Ruck antigens were substituted for the Calmette no fixation was shown in any case.

The sera for this test had not reached more than a few degrees above freezing since they were packed at Asheville; while not frozen, they were very cold on arrival.

May 29, 1914.—Examination of 15 specimens received from Dr. von Ruck, these being in a frozen condition when received. These specimens included five from calves which had received treatment with von Ruck vaccines prepared either from human or bovine type tubercle bacilli and in all of which more or less fixation of complement had been demonstrated at the von Ruck laboratory; two from rabbits with similar treatment and results; and eight from children—two specimens from each of four, one taken before and the other a few days after a dose of the vaccine. In those taken before the administration of the vaccine no more than a trace of fixation had been found, while the specimens taken afterwards had shown considerable fixation.

The tests at the Hygienic Laboratory failed to demonstrate fixation in any of these 15 sera, either by the von Ruck method or by that used at the Hygienic Laboratory which was carried out on 12 of them, using, however, the antigens supplied by Dr. von Ruck.

June 9, 1914.—Examination of six sera shipped by Dr. von Ruck. These were from persons who had received immunizing or curative

treatment with the vaccine or watery extract, and in all of them some degree of fixation had been found at Dr. von Ruck's laboratory. This batch of sera was not examined by Dr. von Ruck's technic, but by our own, using the von Ruck antigens which he had supplied, and, in addition, the antigen which had been prepared and used by Dr. Besredka. No fixation was demonstrated in any case.

Summary.—There were examined by the service representatives about 80 specimens of serum with their controls in an attempt to discover by personal experience what the value of the von Ruck methods of performing complement fixation tests might be. As had been foreseen from the observation of the method as practiced by Dr. von Ruck's assistants, and from a consideration of the theoretical basis of the test, it was found to be untrustworthy, easily swayed by influences aside from the specific reactions sought, and, far from being more expeditious than the apparently more elaborate methods in common use, it was in the end more time-consuming and laborious. Complement fixation plays such an important part in the whole system of the Von Ruck methods that when it, as performed at the von Ruck laboratory, is discredited the whole philosophy of treatment and immunization based upon it must suffer in proportion.

Bacteriolysis.—It is one of the claims of the Doctors von Ruck that the serum of persons and animals treated by their methods acquire the property of exerting lytic action on tubercle bacilli in vitro which can be observed by microscopic examination. Furthermore, that the bacteria can be shown to have been robbed of their virulence by exposure to the action of such sera, by injecting the mixture subcutaneously into guinea pigs, which then fail to develop and die of the disease. The acquisition of this property they regard as indisputable evidence of immunity and this constitutes the most important experimental evidence which they adduce in support of the claim that they can immunize *persons* against tuberculosis.

In a conversation with Dr. Karl von Ruck he told me that he had come to regard the miscroscopic demonstration of lysis as of less importance than he had formerly supposed, inasmuch as he had recently observed that guinea pigs injected with mixtures of "immune" serum and tubercle bacilli, failed to develop tuberculosis even when the microscopic evidence of lysis has been inconclusive. This conversation occurred at a time when I was making almost daily requests to have the phenomenon of lysis demonstrated to me under the microscope. In spite of my repetition of this request on many occasions, never during my entire stay at Asheville was it complied with although entries were being made at the same time on the record books which indicated that plenty of suitable material was available.

From the above facts the inference seems plain that Dr. von Ruck considered the specimens sufficiently conclusive to warrant entry on his permanent records but not to warrant demonstration to me. I was permitted to examine some slides, some of which were said to show lysis. These I found crowded with contaminating organisms and the tubercle bacilli in about the same condition in the test slides and the control slides made from a salt solution suspension, which latter was obtained with some difficulty. I was unable on any occasion to determine that lysis had occurred.

I experienced also great difficulty in ascertaining what the standard echnic was in performing these tests. A statement of this made one ay would be contradicted a few days later, or, without notice to me, hanges would be made in the current practice at the laboratory. 'hese changes, I ascertained, were uniformly in the direction of ncreasing the amount of serum employed, while keeping the amount f tubercle bacilli constant, a fact which indicates that the degree of ysis formerly observed must have been unsatisfactory, in spite of the nicrophotographs in one of Dr. von Ruck's articles which appear to how the phenomenon very beautifully.

The question of technic is so vital that attempts were made to ecure from Dr. Karl von Ruck a statement of what the standard echnic was. On September 22, 1913, he would make no definite eply to such an inquiry, saying that he had plans to improve his resent technic, and following with a discussion of different ways in hich this could be done. The question was renewed on September 9 and the same sort of reply was offered, but since I was about to nake some tests which were to form an important part of the investiation my request was made more insistent and Dr. von Ruck finally ommitted himself to the following statement of procedure:

Add two drops of the inactivated serum to an equal volume of the ubercle bacilli suspension prepared in his laboratory, incubate two ours at 37° C., and then add two drops of the active serum, and omplete 24 hours incubation, when the specimen is ready for microcopic examination or injection into guinea pigs. The tests which I ave performed were done according to this technic up to the time hen it was changed in a communication from Dr. von Ruck about he middle of May, 1914. The change consisted in the use of active erum throughout.

My observations on the technic of lysis tests as employed at the on Ruck laboratory brought out the following points: The suspenion of supposedly virulent tubercle bacilli was made by weighing out mg. of tubercle bacilli and emulsifying this by rubbing by hand in n open agate mortar in a total volume of 10 c. c. of salt solution. 'hese emulsions were frequently kept at room temperature and epeatedly used for as much as a week before being finally discarded. 'he collection of the blood has been described. As a consequence oth were grossly contaminated with microorganisms, and a smear nade from the mixture after 24 hours' incubation would sometimes how perhaps a hundred other bacteria to one tubercle bacillus. Since he control was made with salt solution and not with serum, this slide ould show relatively fewer contaminating bacteria, but all which I ave examined have shown beaded, disintegrated, and shadow forms f the tubercle bacillus in equal degree with the test slides. It seems nnecessary to detail these examinations, since the results have lways been the same. Their total number was considerably more han that of the "lytic" animal experiments detailed below.

Serum No.	Patient treated.	Von Ruck determination of lysis — = none recorded.	G. P. No.	Injected subcutaneously.	Weight when injected.	Weight at time of death.	When died.	Post-mortem findings.
				1913.			1913.	
1	No	—	1	Sept. 21	430	300	Nov. 9	Advanced generalized tuberculosis.
2	No	—	2	...do	530	390	Nov. 12	Do.
3	No	—	3	...do	425	350	Nov. 22	Do.
4	No	—	4	...do	530	420	...do	Do.
Control		—	5	...do	430	390	...do	Do.
5	No	—	17	Oct. 2	300		2 days.	Intercurrent infection.
6	No	—	18	...do	300		1 day.	Do.
7	No	—	19	...do	300	870	Killed Sept. 11	No gross lesions.
8	No	—	20	...do	315			Pig lost.
9	Yes	—	21	...do	315		1 day.	Intercurrent infection.
10	Yes	—	22	...do	315		...do	Do.
11	No	—	23	...do	310		3 days.	Do.
12	No	—	24	...do	310		7 days.	Do.
13	No	—	25	...do	305	1,000	Killed Sept. 11.	No gross lesions.
14	No	—	26	...do	305	280	Killed Dec. 6.	Extensive slough. Beginning tuberculosis of spleen. (?)
Control			27	...do	310	1,130	Killed Sept. 11.	No gross lesions.
Do			28	...do	310	1,100	...do	Do.
							1914.	
16	No	—	29	Oct. 6	290	385	Jan. 24	Advanced generalized tuberculosis.
17	No	—	30	...do	320	475	Jan. 13	Advanced generalized tuberculosis. Death precipitated by hemorrhage.
18	Yes	—	31	...do	315	365	Jan. 3	Advanced generalized tuberculosis.
19	Yes	—	32	...do	300	340	Jan. 20	Do.
20	Yes	—	33	...do	315	355	Nov. 20	Pneumonia and beginning tuberculosis of lungs, liver, and spleen
21	Yes	—	34	...do	305	575	Apr. 21	Advanced generalized tuberculosis. Extensive dropsy accounts for weight.
Control			35	...do	320	445	Mar. 18	Advanced tuberculosis. Lungs not macroscopically involved.
Do			36	...do	320	400	Jan. 21	Pneumonia. Tuberculosis of liver and spleen
				1914.				
V. R. 2	Yes	+	52	May 15	300	250	79 days.	Advanced generalized tuberculosis.
5	Yes	+	53	...do	285	270	146 days.	Do.
6	Yes	+	54	...do	300	270	90 days.	Do.
7	Yes	0	55	...do	270	305	99 days.	Do.
10	Yes	+	56	...do	300	290	83 days.	Do.
11	Yes	+	57	...do	295	440	162 days.	Advanced tuberculosis.
12	Yes	+	67	...do	300	375	(1)	Do.
13	Yes	0	58	...do	300	340	150 days.	Advanced generalized tuberculosis.
14	Yes	+	59	...do	290	470	(1)	Moderately advanced tuberculosis.
15	Yes	+	60	...do	290	360	139 days.	Advanced generalized tuberculosis.
16	Yes	+	61	...do	300	415	(1)	Advanced tuberculosis.
19	Yes	+	62	...do	300	245	58 days.	Moderate tuberculosis of liver and spleen. T.B. demonstrated.
20	Yes	+	63	...do	290	435	148 days.	Advanced generalized tuberculosis.
29	Yes	+	64	...do	300	320	138 days.	Do.
30	Yes	0	65	...do	290	220	100 days.	Do.
41	Yes	2+	66	...do	290	225	80 days.	No post mortem.
43	Yes	3+	68	...do	300	275	79 days.	Advanced generalized tuberculosis.
44	Yes	3+	69	...do	300	345	123 days.	Do.
47	Yes	3+	70	...do	300	230	101 days.	Do.
49	Yes	3+	71	...do	300	270	85 days.	Do.
50	Yes	3+	72	...do	300	300	78 days.	Do.
51	Yes	3+	73	...do	300	410	146 days.	Do.
52	Yes	3+	74	...do	300	260	108 days.	Do.
Control			[2] 75	...do	280	385	155 days.	Do.
Do			[3] 76	...do	270	375	150 days.	Do.

[1] Killed, 162 days. [2] Normal serum control, Hygenic Laboratory. [3] Salt solution control.

Considerable information is contained in these tables besides that relating to the question of whether the serum of treated persons is really lytic or not.

The first series was entirely composed of tests on untreated persons. In this no evidence of lysis was to be expected. The inoculations were made at Asheville and the animals shipped later to Washington. The second series (5 to 14) was made also with an emulsion furnished by Dr. von Ruck's assistant, but on the completion of the incubation the tubes were sealed off and shipped to Washington, where the injections were made. Owing to the great contamination of the serum in this series about half the animals died within a few days of acute infection. Those which survived, however, reached a great weight before they were killed nearly a year later, when no evidence of tuberculosis was found. The emulsion furnished was evidently avirulent.

A marked difference is noted in the virulence of the two emulsions of tubercle bacilli prepared at the Asheville laboratory and handed to the service representatives at an interval of 11 days for test purposes. The first was fully virulent, the second apparently avirulent. The method of keeping (or rather of neglecting) these important emulsions current at the von Ruck laboratory is a possible explanation of the great fluctuations in virulence of their test cultures observed by us and complained of by Dr. von Ruck and made the basis of his inability to demonstrate certain of his results. It is also a possible explanation of some of the early results which led Dr. von Ruck to place so much reliance on the efficacy of his vaccine.

The third series (16 to 21) was prepared from a culture in my own possession shipped from Washington, in a cleanly manner, and after incubation the tubes were sent to the Hygienic Laboratory for injection. No premature deaths occurred in this series. Serums Nos. 18 to 21 were from children who had received immunizing treatment some time previously, and the animal injected with the tube contents from one of them lived a month longer than the best control, an isolated result having little significance.

The third series, in which we have the advantage of Dr. von Ruck's own determinations of lysis by microscopic examination, shows no correlation between them and the length of life of the animals. There is thus no evidence that the serum of treated persons can destroy the virulence of the tubercle bacillus in vitro, while there is, it appears, sufficient evidence that it can not do so.

Tests for agglutinins, precipitins, and opsonins.—I am not disposed to criticise the technic employed by Dr. von Ruck in carrying out these tests as stringently as I have been obliged to criticise the fixation and lysis technics. The opsonin technic I never saw used at Asheville and I believe it was very seldom employed.

The agglutination test was made by exposing an emulsion of avirulent tubercle bacilli in carbolized salt solution, made by prolonged trituration by hand in an agate mortar, to the action of various dilutions of the serum at 37° for 48 hours, the tubes being placed in a slanting position. A clearing of the opalescent upper portion of the liquid with the deposit of finely granular material on the lower side of the tube constituted a positive reaction. This was often difficult to determine, since the emulsions varied much in density and a considerable deposit often occurred in the control tubes with no serum.

Considerable play of the personal equation and the individual judgment was permitted in reading these tests. My experience with these tests is too limited to warrant an expression as to the value of Dr. von Ruck's contentions concerning them. At any rate, they are of inferior importance in his system.

The reagent used for the precipitin tests is the von Ruck watery extract or one of his protein solutions. Serum is added to this in progressive dilutions, and after incubation the test is read by tapping the loosely held tube and looking for a delicate cloudy precipitate which arises from the bottom in cases of positive reaction. Tests which I made parallel to some made by Dr. von Ruck's assistants gave readings quite at variance with their tests. Dr. von Ruck's contention is that the precipitin reaction runs inversely to the other reactions and to the well-being of the patient. Such work as has been reported by other observers is contrary to this contention and so also was my own. For example, of 15 patients who had not received treatment I found but 1 in which the precipitin titer exceeded 1/200, while 3 of 6 treated persons gave a titer greater than 1/200.

The immunization of animals by the von Ruck vaccine.—One of the most important pieces of evidence as to the efficacy of his vaccine is the claim that by its use he is able to so immunize guinea pigs that when these are subsequently injected with virulent tubercle bacilli they fail to succumb to the infection, as do the untreated control animals, and continue to gain weight and to thrive. If they are killed and a post-mortem examination is made, one is said to find, at most, scanty and encapsulated lesions, such as are observed after the injection of dead tubercle bacilli. Dr. von Ruck told me that it required a variable time to accomplish this degree of immunity, but in general from 6 to 10 weeks. The dose, he said, was 1/5 mg. (i. e., total solids) per 100 gm. weight of guinea pig, given subcutaneously in several fractions at different portions of the abdominal wall to favor a better absorption; this dose to be repeated weekly.

At another time he recommended doubling the dose in order to obtain immunity at an earlier date. It could be told when the animals had reached a proper degree of immunity, he said, by examining the blood serum until a high degree of complement fixation and of lysis was discovered.

Dr. von Ruck had already severely criticized the experiment made by Dr. Cummings, of California, on the ground that this investigator had not made use of these serum tests in determining when the animals had reached a sufficient degree of immunity to justify their being subjected to virulent inoculation. This situation is discussed from Dr. von Ruck's standpoint in a pamphlet entitled "The failure of Dr. R. S. Cummings to protect guinea pigs against tuberculous infection with the vaccine of Dr. Karl von Ruck," dated at Asheville July 19, 1913. In this pamphlet Dr. von Ruck displays considerable bitterness regarding the manner of performance of Dr. Cummings's tests, and says, in effect, that the cause of failure lay in not determining the immunity of the animals by serum tests before giving the virulent inoculation.

Subsequently Dr. von Ruck stated to me that he was convinced that the old batch of vaccine (the same as that used by Dr. Cum

mings) had deteriorated so that he was not able to immunize animals with it.

The real cause of Dr. Cummings's failure would therefore seem to lie, not so much in his omission of the serum tests, as in the deterioration of the vaccine, if indeed it had ever possessed the immunizing properties which Dr. von Ruck thought to have demonstrated.

We were afforded an opportunity of testing an entirely new batch of vaccine assembled about September 1, 1913, and believed by Dr. von Ruck, on the basis of its method of preparation and the results of chemical examination, to closely correspond with the "old" batch when it was freshly made and when it was said to be potent. This we applied according to Dr. von Ruck's instructions as to dosage and intervals.

The first series which we attempted to treat in this manner were given the double dose recommended by Dr. von Ruck. The animals soon became sick and lost weight and some of them died, so that we were obliged to start another series, employing only the single dose which at first was recommended. The animals did well under the course of treatment. Like Dr. Cummings, we did not attempt to determine the state of immunity by serum tests, being influenced by three reasons: First, we had no confidence in the technic of this test as applied by Dr. von Ruck and the amounts of serum obtainable from the guinea pig's ear were too small to perform more suitable tests; second, the repeated taking of specimens would probably injure the animals and invalidate the tests; third and chiefly, we were not interested in this experiment in the demonstration of antibodies by serum tests, our problem being whether or not it was possible to immunize guinea pigs by various courses of treatment with the von Ruck vaccine.

The number of injections given in this series varied from a minimum of 9 to a maximum of 18. When the animals were given the inoculation of virulent tubercle bacilli, untreated animals were similarly inoculated to act as controls. The table following shows the conditions and results of the experiment.

Attempt to immunize guinea pigs.—These were all healthy young animals from stock raised in the Hygienic Laboratory in which no instances of spontaneous or of pseudotuberculosis has ever been observed. They were given 0.02 c. c. of the vaccine intended for animal experiment, corresponding to the batch finished about September 1, 1913, for each 100 gm. of weight of the animal at the time of injection. This dose, diluted in salt solution, was divided into four portions which were injected at different places on the abdominal wall. It is the dose originally recommended verbally to me by Dr. von Ruck. The injections were repeated every week or 10 days. The animals were weighed regularly. They all exhibited a good gain in weight during the treatment, and subsequent to virulent infection the weights followed the course usual in tubercular infections. The treatments were begun on November 29, 1913. The control animals were healthy animals from the same stock, as nearly as possible of the same weight as the test animals. Their inoculation was in all respects the same as that of the tests. This consisted of 0.1 mg. of a human strain grown on potato injected subcutaneously into the right flank.

G. P. No.	Doses vaccine.	Duration treatment.	Weights.			Date inoculated.	Died, later days.	Post-mortem findings.
			Original.	Inoculated.	Death.			
41	16.....	17 weeks..	445	840	690	1914. Mar. 31	84	Ulcer, right groin. Lymph nodes enlarged and caseous. Advanced tuberculosis of spleen, liver, and lungs.
41A	Control...	.....	.....	880	850	...do.....	39	Body fat. Recent abortion. Mediastinal gland size of cherry. Moderate tuberculosis of spleen and liver, none of lungs.
41B	Control...	.....	.....	810	785	...do.....	124	Tuberculosis of liver, lungs, and lymph nodes. Spleen little involved.
42	14.....	16 weeks..	375	775	610	Mar. 23	45	Advanced tuberculosis of liver and spleen. Few tubercles in lungs. Enlarged and caseous lymph nodes.
42A	Control...	.....	.....	750	630	...do.....	120	Advanced generalized tuberculosis. Caseation of lymph nodes.
42B	Control...	.....	.....	750	620	...do.....	120	Do.
43	11.....	11 weeks..	425	590	490	Feb. 18	66	Emaciated. Advanced tuberculosis of spleen, liver, and lungs. Lymph nodes caseous. Pleuræ full of fluid.
43A	Control...	.....	.....	580	630	...do.....	103	Emaciated. Advanced tuberculosis of spleen, liver, and lungs. Lymph nodes caseous. Pleuræ full of fluid. Abdominal hemorrhage immediate cause of death.
43B	Control...	.....	.....	610	480	...do.....	158	Post mortem lost; pig cremated by mistake.
44	16.....	17 weeks..	470	770	620	Apr. 6	62	Advanced tuberculosis of spleen, liver, and lungs. Moderate enlargement of lymph nodes, dry caseation in one.
44A	Control...	.....	.....	720	490	...do.....	124	Advanced tuberculosis of spleen, liver, and lungs. Lymph nodes caseous.
44B	Control...	.....	.....	750	505	...do....	96	Do.
45	10.....	10 weeks..	445	570	600	Feb. 9	212	Not emaciated. Ulcer right groin and caseous gland. Advanced tuberculosis of spleen, liver, and lungs, which all contain tubercle bacilli. Fibroid and fresh lesions present.
45A	Control...	.....	.....	530	565	...do....	74	Advanced tuberculosis of spleen, liver, and lungs, caseous lymph nodes and ulcer. Decomposed fetuses in uterus.
45B	Control...	.....	.....	580	465	...do....	51	Emaciated. Tuberculosis of spleen, liver, and lungs. Two big abscesses in abdominal cavity. Peritoneum covered with fibrinous exudate.
46	11.....	11 weeks..	405	620	540	Feb. 24	56	Advanced tuberculosis of spleen and liver, moderate of lungs. Caseous lymph nodes. Big caseous abscess in neck.
46A	Control...	.....	.....	605	670	...do....	56	Atypical lesions of spleen and liver, caseous gland right groin. Other organs enlarged and surrounded by edema, suggesting acute process. Smears show few tubercle bacilli and many diplococci.
46B	Control...	.....	.....	575	435	...do....	104	Advanced generalized tuberculosis. Caseous lymph nodes.

G. P. No.	Doses vaccine.	Duration treatment.	Weights.			Date inoculated.	Died, later days.	Post-mortem findings.
			Original.	Inoculated.	Death.			
47	18.....	19+weeks.	415	660	540	Apr. 27	87	Advanced tuberculosis of spleen, liver, and lungs. Caseous lymph nodes. Subinoculations cause death from tuberculosis in 49 and 69 days in 2 pigs, respectively.
47A	Control ...	.....	.....	870	660	...do....	84	Same findings as No. 47.
48	18.....	19+weeks.	425	725	640	...do....	62	Inguinal and axillary nodes caseous. Moderate tuberculosis of spleen, liver, and lungs. Enormous retroperitoneal abscess in abdomen and right pyelitis due to pressure on ureter. Tubercle bacilli in major organs.
48A	Control ...	.....	.....	790	620	...do....	157	Advanced tuberculosis of major organs not as extreme as in many of the series. Acute nephritis. Peritoneal fluid increased.
49	12.....	12 weeks..	445	650	595	Mar. 2	116	Advanced tuberculosis of spleen, liver, and lungs. Caseous nodes. Enormous caseous abscess of retroperitoneal origin.
49A	Control ...	.....	.....	680	540	...do....	96	Advanced tuberculosis of spleen, liver, and lungs. Caseous lymph nodes.
49B	Control ...	.....	.....	630	600	...do....	105	Advanced tuberculosis of spleen, liver, and lungs. Caseous lymph nodes, and free fluid in peritoneum and pleuræ.
50	9.....	9 weeks...	380	515	350	Jan. 31	64	Advanced tuberculosis of spleen, liver, and lungs and omentum.
50A	Control ...	.....	.....	500	440	...do....	94	Same, except omentum.
50B	Control ...	.....	.....	560	540	...do....	25	Caseous lymph nodes and focus in musculature of left abdominal wall. Tubercles on spleen, which is not enlarged. Few small foci in liver. Lungs congested, but not tuberculous.

A consideration of this table gives no evidence that the animals eceiving the Von Ruck vaccine were immune to tuberculosis. One, is true, lived far longer than its own controls, in each of which, owever, there was good reason to believe that intercurrent condiions had hastened death, and longer than any other control in the eries. Nevertheless, it died of tuberculosis and exhibited active esions containing numerous tubercle bacilli at necropsy. This nimal, it is to be noted, had received but 10 injections. Other aniials which had received approximately the same number of injecions showed no such prolongation of life, nor did those which got uch longer treatment.

On the whole, even including this animal which lived 212 days, he average duration of life in the treated animals was much shorter han in the controls (84.4: 96.1 days) and a just elimination from onsideration of those animals in which intercurrent conditions could onfidently be assumed to have hastened death only serves to exagerate the discrepancy. If this case and its controls be eliminated, he average duration of life in treated and untreated animals becomes 1.3 and 100.3 days, respectively, so that we are forced to the con-

clusion, so far as these tests will permit of such, that if we are to deduce that the treatment succeeded in prolonging the life of one animal, we must also admit that it shortened the lives of the other nine.

I am well aware that this experiment is open to the objection that Dr. von Ruck's contention that the immunity of the animals should be demonstrated by serological methods before proceeding to the final test of virulent inoculation has not been complied with. However, this decisive test having shown that the animals were not immunized, it is a matter of indifference to me what degree of supposed immunity they might have shown by serological methods.

Dr. von Ruck's records.—Having been repeatedly criticized by Dr. von Ruck for failure to avail myself of the very extensive records which he has accumulated regarding clinical and experimental observations, I shall give in detail the incident which, above other things, deterred me from examining them. Curiously this has to do with his current records, which were being accumulated at the time of my observations in Asheville.

On August 25, 1913, a test was made by Dr. von Ruck's assistant on the sera of some fifty-odd children who had received "immunizing" treatment at the Thomasville Orphanage during the previous year. The object of the test was to demonstrate that even after the lapse of this time "immune" antibodies could still be demonstrated in the serum. The tests were not completed until late in the evening, and, being detained at the laboratory myself, I asked permission to examine the tubes after the men had finished reading them. This was of course granted and the men having in the meantime left, while I was finishing another experiment, I had to refer to the records in order to determine what their interpretation had been of certain results. Before leaving, one of the men had referred apologetically to the lack of controls in certain cases, saying that there was only enough serum to run serum-control tubes on about half the sera. I did not examine all the tests, but in a portion of them I found that although serum controls had been made, the results as entered in the book failed to mention the lack of hemolysis in the control tube as observed by me. This had the effect of making it appear on the records that "immune" antibodies were still present in the patient's serum, whereas in reality no conclusion was justified except that the serum exhibited of itself anticomplementary properties, as highly contaminated serum is apt to do. I append a table showing the discrepancies alluded to, substituting numbers of my own for the names of the patients.

Patient.	The von Ruck book. Fixation.				My observations on the serum control.[1]
	P2	TB.	NF.	FA.	
1	0	4	0	0	Almost complete checking.
2	+	4+	4+	+	Half hemolysis.
3	4	4	+	+	Slight hemolysis.
4	0	4	+	0	Half hemolysis.
5	4	8	4	+	Same as P2, NF, and FA 1/4.
6	+	+	+	+	Do.
7	4	4	+	+	No hemolysis; same as TB 1/4.

[1] The "serum control" is the tube containing the serum to be tested, *without* antigen.

This was brought to Dr. von Ruck's attention the next morning.

On September 3, 1913, I discovered, on looking over the record book, that certain entries had been made opposite certain of the tests made on August 25, since the time when I had made the notes on them as given above. These new entries were:

Patient.

8, 9, 10 } "Slight check in control."

11, 12, 1, 2 } "No serum control."

There were but five original entries indicating that the serum-control tube had shown incomplete hemolysis.

To sum up the discrepancies between the records and the facts:

Entries on book.	Facts observed.
5 cases where controls "checked".....	7 additional cases where controls checked.
3 cases where controls slightly "checked".	
4 cases marked "no serum control".....	The assistant in charge of the test had said that there was only enough serum to run serum controls on about half of the cases. Since there were over 50 cases, there must have been approximately 25 without controls, if his statement was correct.
Among the above appear cases 1 and 2....	I had personally seen control tubes for No. 1 and No. 2, and made notes on the fact that they showed incomplete hemolysis.

The attempts to readjust the records in order to give a semblance of consideration to the absence of, or checking in, the controls had consequently been made either from faulty memory or in a chance manner, or possibly by selection. Some basis for the last interpretation may possibly be found in the fact that the cases thrown out of consideration by the emendations had been those in which little "fixation" had occurred. At any rate, these observations had the effect of removing the entire test from my consideration as a scientific proceeding and naturally rendered me very skeptical as to the scientific value of the records of previous tests.

In view of Dr. von Ruck's recently expressed conviction that he had been deceived by certain of his assistants as to the manner in which some of his earlier experimental work had been done, one can not refrain from remarking how much trouble he could have spared himself by a thorough and impassionate investigation when the above facts were brought to his attention.

Clinical observations.—I have made no clinical observations on human beings which enable me to form from this source an opinion as to whether or not the von Ruck methods are efficient in immunizing against or in favorably influencing the course of tuberculosis. The difficulties attending such an investigation are well known and consist principally of the interplay of factors which can not be controlled and are extraneous to the central question.

Among these are the tendency of tuberculous cases to fluctuate widely in their physical condition from month to month without definitely assignable cause, and in certain types to make apparent recoveries or to improve greatly without specific treatment when placed under favorable circumstances; the difficulty of determining

when an arrest of the disease or a recovery has taken place, and the difficulty of assigning their true values to processes which are purely tuberculous, and those which are in the nature of complications or result from permanent damage due to antecedent tuberculous processes. For example, if a child suspected of tuberculous tendency from known association with active cases and the possession of a delicate physique were to receive immunizing treatment and thereafter exhibited a rather remarkable bodily improvement, it would be necessary to rule out other concurrent possible causes of improvement—the relief of adenoids, of hookworm infection, the treatment of hereditary syphilitic taint, improved food or hygienic surroundings, etc., before one would be justified in ascribing the improvement to the treatment. In the case of the treatment of developed tuberculosis this elimination becomes still more difficult.

I have only to cite the case of tuberculin to prove this argument. This product, one like the von Ruck vaccine prepared from the tubercle bacillus, has been before the medical profession for something like 30 years and the opportunity of experimenting with it has been most widely indulged, and yet the indications for its use, the method of its application, and the ultimate results to be expected from it are still the subjects of controversy, and the final verdict has not been rendered save in one particular; it is generally admitted that tuberculin, except when skillfully administered, is a dangerous thing; that its injudicious use may result in catastrophy.

It is essential therefore that any product resembling tuberculin should be carefully scrutinized for possible dangerous properties before it is turned over to the medical profession for the rather indiscriminate use which it is sure to receive at first.

From a consideration of its reported composition there can be no doubt that such a scrutiny is clearly called for before any one's statement of alleged advantages of the product is to be made the basis of its wide employment. Dr. von Ruck states that the vaccine is harmless; yet he does not employ the vaccine in every case, nor in all stages of the disease, nor always in full doses, either because he does not consider it indicated at the time or because, as he acknowledges, it may cause abscesses or give rise to unpleasant evidences of increased activity.

I made some observations at Asheville which are worthy of record in this connection: Four children of a tuberculous parent were subjected to a von Pirquet test. Three gave definitely positive reactions of varying severity while the fourth gave a dubious or negative reaction. The children were then given a dose of vaccine and I saw them a few days later. All three who had had a positive von Pirquet reaction had suffered, following the injection of vaccine, with headache, febrile sensations, some nausea, sleeplessness, and much discomfort in the arms at the site of injection. Their arms showed red areas around the needle puncture about 3 inches in diameter, the skin being somewhat swollen. The other child, however, who had not given a positive von Pirquet reaction, had had no discomfort, and there was only a slight blush at the site of injection.

As might be expected, persons who react positively to tuberculin react in a similar manner to the von Ruck vaccine. It is therefore quite probable that the latter is capable of causing the same focal reactions which constitute a serious danger in the use of tuber-

ulin. Some proof that this is not the case, beyond the mere statenent that the vaccine is not dangerous, should be demanded by the hysician making use of this product.

CONCLUSIONS.

This report concerns itself with the methods and practices of Drs. Karl and Silvio von Ruck as applied to the prevention and cure f tuberculosis during the time of the investigation and not as to what hey may have been at some previous time or what the prospects of heir future may be.

At the time of the investigation the Drs. von Ruck were unable o furnish evidence of a satisfactory nature in support of their conentions regarding certain fundamental phenomena upon which their ystem of specific therapy is based. Nor were the investigators able, y independent experiments, to confirm the claims made by the Drs. von Ruck regarding these phenomena.

On the other hand, evidence was elicited to the effect that the accine, around which this investigation centers, is constructed on the asis of tests which are faulty in theory and in practice and are nreliable. The chances that the vaccine represents a combination nore perfect than similar preparations used in connection with uberculosis are therefore remote. It has been admitted by Dr. von Ruck that the vaccine is unstable, subject to deterioration, and mpossible of duplication with certainty. Its potency can not, therefore, be standardized for practical purposes since, by the time the esults of the protracted tests become known, deterioration may have ccurred.

We have been unable to immunize guinea pigs against virulent tuberular injections by the use of the vaccine in doses recommended by Dr. Karl von Ruck and continued for the length of time, and longer, which he reports as adequate for this purpose. On the contrary, nost of our animals so treated exhibited increased susceptibility.

We have been unable to demonstrate that the serum of persons r animals treated with the vaccine, and said by Dr. von Ruck o possess the necessary immune antibodies, is competent to destroy he virulence of the tubercle bacillus. Our evidence shows that such erum is not competent to do so.

It has been impossible to collect direct evidence bearing on the uestion of whether the vaccine used by the Drs. von Ruck, in ttempting to render persons in health immune to tuberculosis, is uccessful or not in immunizing those thus vaccinated. The indirect vidence offered by the Drs. von Ruck in proof of the success of the accine in producing immunity has been found to be inadequate nd faulty.

A consideration of the composition of the vaccine, and of the effects aid and observed immediately to follow its use, lead one to anticipate hat its reaction would be similar to that of the preparations known enerically as tuberculins without there being particular reasons or anticipating any especial advantages of comparative freedom from anger on the part of the vaccine.

Aside from the employment of the vaccine and other specific herapeutic agents by the Drs. von Ruck, their methods are modern nd comprise those generally employed in the best sanatorium ractice.

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